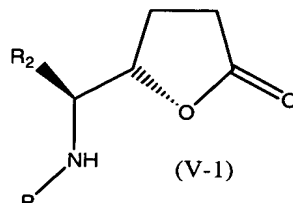


What is claimed is:

1. A method of making a compound of the formula (V-1):



- 5 wherein:

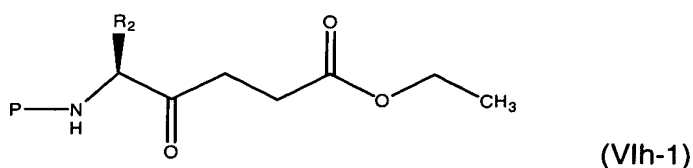
P is a protecting group;

- R₂ is phenyl-(CH₂)_m-, naphthyl-(CH₂)_m-, (C₃-C₁₀)cycloalkyl-(CH₂)_m-, (C₁-C₆)alkyl or (C₂-C₉)heteroaryl-(CH₂)_m-, wherein each of said phenyl, naphthyl, (C₃-C₁₀)cycloalkyl or (C₂-C₉)heteroaryl moieties of said phenyl-(CH₂)_m-, naphthyl-(CH₂)_m-, (C₃-C₁₀)cycloalkyl-(CH₂)_m- or (C₂-C₉)heteroaryl-(CH₂)_m- groups may be optionally substituted with one, two, or three substituents independently selected from the group consisting of hydrogen, halogen, CN, (C₁-C₆)alkyl, hydroxy, hydroxy-(C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, HO-(C=O)-, (C₁-C₆)alkyl-O-(C=O)-, HO-(C=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-O-(C=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-(C=O)-O-, (C₁-C₆)alkyl-(C=O)-O-(C₁-C₆)alkyl, H(O=C)-, H(O=C)-(C₁-C₆)alkyl, (C₁-C₆)alkyl(O=C)-, (C₁-C₆)alkyl(O=C)-(C₁-C₆)alkyl, NO₂, amino, (C₁-C₆)alkylamino, [(C₁-C₆)alkyl]₂amino, amino(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)alkyl, [(C₁-C₆)alkyl]₂amino(C₁-C₆)alkyl, H₂N-(C=O)-, (C₁-C₆)alkyl-NH-(C=O)-, [(C₁-C₆)alkyl]₂N-(C=O)-, H₂N(C=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-HN(C=O)-(C₁-C₆)alkyl, [(C₁-C₆)alkyl]₂N-(C=O)-(C₁-C₆)alkyl, H(O=C)-NH-, (C₁-C₆)alkyl(C=O)-NH, (C₁-C₆)alkyl(C=O)-[NH](C₁-C₆)alkyl, (C₁-C₆)alkyl(C=O)-[N(C₁-C₆)alkyl](C₁-C₆)alkyl, (C₁-C₆)alkyl-S-, (C₁-C₆)alkyl-(S=O)-, (C₁-C₆)alkyl-SO₂-, (C₁-C₆)alkyl-SO₂-NH-, H₂N-SO₂-, H₂N-SO₂-(C₁-C₆)alkyl, (C₁-C₆)alkylHN-SO₂-(C₁-C₆)alkyl, [(C₁-C₆)alkyl]₂N-SO₂-(C₁-C₆)alkyl, CF₃SO₃-, (C₁-C₆)alkyl-SO₃-, phenyl, phenoxy, benzyloxy, (C₃-C₁₀)cycloalkyl, (C₂-C₉)heterocycloalkyl, and (C₂-C₉)heteroaryl; and

m is 0, 1, 2, 3, or 4;

wherein the method comprises:

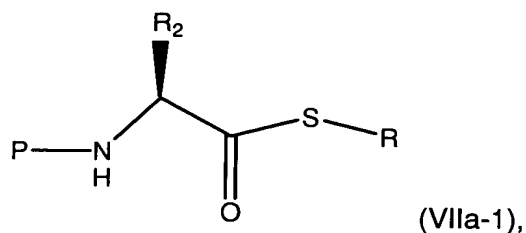
- a) reacting a compound of the formula (VIh-1)



with a reducing agent, and

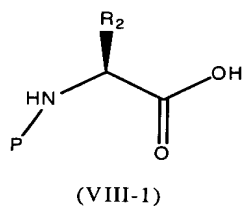
c) cyclizing the compound so formed with heat and an acid catalyst.

- 5 2. The method of claim 1, further comprising formation of the compound of the formula (VIh-1) by reacting a compound of the formula (VIIa-1)



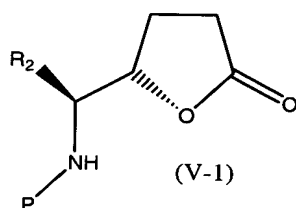
wherein R is a (C₁-C₂₀)alkyl, (C₃-C₁₀)cycloalkyl, aryl, or (C₂-C₉)heteroaryl with an organozinc compound in the presence of a palladium catalyst and a racemization scavenger.

3. The method of claim 2, further comprising formation of the compound of the formula (VIIa-1) by reacting a compound of the formula (VIII-1)



- 15 with a compound of the formula HS-R.

4. A method of making a compound of the formula (V-1):



wherein:

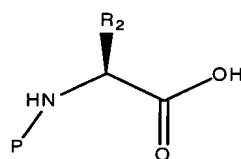
- 20 P is a protecting group;

R_2 is phenyl-(CH₂)_m-, naphthyl-(CH₂)_m-, (C₃-C₁₀)cycloalkyl-(CH₂)_m-, (C₁-C₆)alkyl or (C₂-C₉)heteroaryl-(CH₂)_m-, wherein each of said phenyl, naphthyl, (C₃-C₁₀)cycloalkyl or (C₂-C₉)heteroaryl moieties of said phenyl-(CH₂)_m-, naphthyl-(CH₂)_m-, (C₃-C₁₀)cycloalkyl-(CH₂)_m- or (C₂-C₉)heteroaryl-(CH₂)_m- groups may be optionally substituted with one, two, or three substituents independently selected from the group consisting of hydrogen, halogen, CN, (C₁-C₆)alkyl, hydroxy, hydroxy-(C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, HO-(C=O)-, (C₁-C₆)alkyl-O-(C=O)-, HO-(C=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-O-(C=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-(C=O)-O-, (C₁-C₆)alkyl-(C=O)-O-(C₁-C₆)alkyl, H(O=C)-, H(O=C)-(C₁-C₆)alkyl, (C₁-C₆)alkyl(O=C)-, (C₁-C₆)alkyl(O=C)-(C₁-C₆)alkyl, NO₂, amino, (C₁-C₆)alkylamino, [(C₁-C₆)alkyl]₂amino, amino(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)alkyl, [(C₁-C₆)alkyl]₂amino(C₁-C₆)alkyl, H₂N-(C=O)-, (C₁-C₆)alkyl-NH-(C=O)-, [(C₁-C₆)alkyl]₂N-(C=O)-, H₂N(C=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-HN(C=O)-(C₁-C₆)alkyl, [(C₁-C₆)alkyl]₂N-(C=O)-(C₁-C₆)alkyl, H(O=C)-NH-, (C₁-C₆)alkyl(C=O)-NH, (C₁-C₆)alkyl(C=O)-[NH](C₁-C₆)alkyl, (C₁-C₆)alkyl(C=O)-[N(C₁-C₆)alkyl](C₁-C₆)alkyl, (C₁-C₆)alkyl-S-, (C₁-C₆)alkyl-(S=O)-, (C₁-C₆)alkyl-SO₂-, (C₁-C₆)alkyl-SO₂-NH-, H₂N-SO₂-, H₂N-SO₂-(C₁-C₆)alkyl, (C₁-C₆)alkylHN-SO₂-(C₁-C₆)alkyl, [(C₁-C₆)alkyl]₂N-SO₂-(C₁-C₆)alkyl, CF₃SO₃-, (C₁-C₆)alkyl-SO₃-, phenyl, phenoxy, benzyloxy, (C₃-C₁₀)cycloalkyl, (C₂-C₉)heterocycloalkyl, and (C₂-C₉)heteroaryl; and

m is 0, 1, 2, 3, or 4;

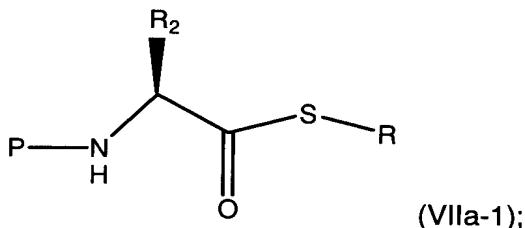
wherein the method comprises:

a) reacting a compound of the formula (VIII-1)



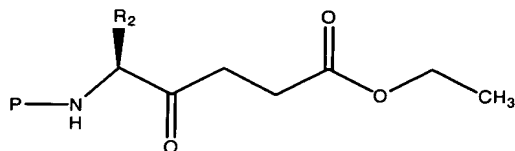
(VIII-1)

with a compound of the formula HS-R, wherein R is a (C₁-C₂₀)alkyl, (C₃-C₁₀)cycloalkyl, aryl, or (C₂-C₉)heteroaryl, to form a compound of the formula (VIIa-1)



(VIIa-1);

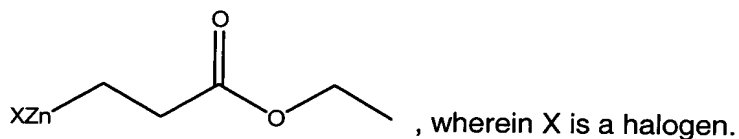
b) reacting the compound so formed with an organozinc compound in the presence of a palladium catalyst and a racemization scavenger to form a compound of the formula (VIh-1)



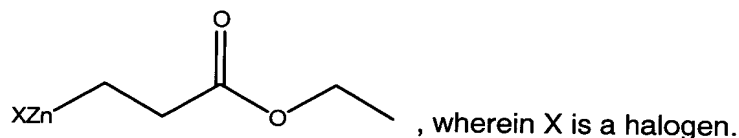
(VIh-1);

- 5 c) reacting the compound so formed with a reducing agent; and
e) cyclizing the compound so formed with heat and an acid catalyst.

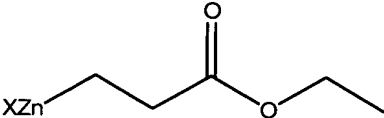
5. The method of claim 2, wherein with the organozinc compound has the formula formula $X-Zn-(C_1-C_6)alkyl-(C=O)-O-R$, wherein X is a halogen and R is a (C₁-
10 C₂₀)alkyl, (C₃-C₁₀)cycloalkyl, aryl, or (C₂-C₉)heteroaryl.



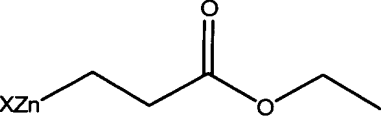
6. The method of claim 4, wherein with the organozinc compound has the formula formula $X-Zn-(C_1-C_6)alkyl-(C=O)-O-R$, wherein X is a halogen and R is a (C₁-
15 C₂₀)alkyl, (C₃-C₁₀)cycloalkyl, aryl, or (C₂-C₉)heteroaryl.



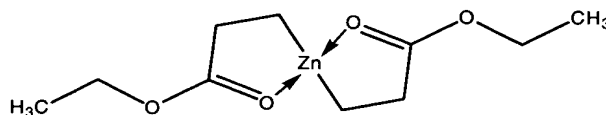
7. The method of claim 2, wherein with the organozinc compound has the

20 formula , wherein X is a halogen.

8. The method of claim 4, wherein with the organozinc compound has the

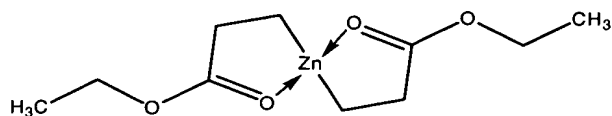
formula , wherein X is a halogen.

9. The method of claim 2, wherein the organozinc compound has the formula



5

10. The method of claim 4, wherein the organozinc compound has the formula



- 10 11. The method of claim 2, wherein the racemization scavenger is a carboxylic acid anhydride or a carboxylic acid ester.

12. The method of claim 4, wherein the racemization scavenger is a carboxylic acid anhydride or a carboxylic acid ester.

- 15 13. The method of claim 2, wherein the racemization scavenger has the formula aryl-(C=O)-O-(C=O)-aryl, R-(C=O)-O-aryl, or aryl-(C=O)-O-aryl.

14. The method of claim 4, wherein the racemization scavenger has the formula aryl-(C=O)-O-(C=O)-aryl, R-(C=O)-O-aryl, or aryl-(C=O)-O-aryl.

20

15. The method of claim 13, wherein the racemization scavenger is phthalic anhydride, 4-nitrophenyl acetate, or 4-fluorophenyl acetate.

16. The method of claim 14, wherein the racemization scavenger is phthalic anhydride, 4-nitrophenyl acetate, or 4-fluorophenyl acetate.

25

17. The method of claim 1, wherein P is carbobenzyloxy, t-butoxy carbonyl or 9-fluorenyl-methylenoxycarbonyl.

18. The method of claim 4, wherein P is carbobenzyloxy, t-butoxy carbonyl or 9-fluorenyl-methylenoxycarbonyl.

19. The method of claim 1, wherein P is t-butoxy carbonyl.

5

20. The method of claim 4, wherein P is t-butoxy carbonyl.

21. The method of claim 1, wherein R_2 is phenyl- $(CH_2)_m$ - or (C_2-C_9) heteroaryl- $(CH_2)_m$ -, wherein each of said phenyl or (C_2-C_9) heteroaryl moieties may be optionally substituted with one, two, or three substituents independently selected from the group consisting of hydrogen, halogen, CN, (C_1-C_6) alkyl, or hydroxy.

22. The method of claim 4, wherein R_2 is phenyl- $(CH_2)_m$ - or (C_2-C_9) heteroaryl- $(CH_2)_m$ -, wherein each of said phenyl or (C_2-C_9) heteroaryl moieties may be optionally substituted with one, two, or three substituents independently selected from the group consisting of hydrogen, halogen, CN, (C_1-C_6) alkyl, or hydroxy.

23. The method of claim 1, wherein R_2 is 3-fluoro-benzyl.

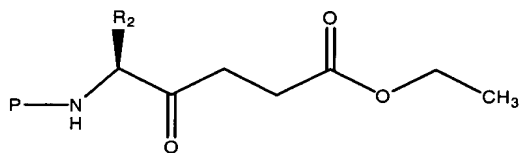
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24. The method of claim 4, wherein R_2 is 3-fluoro-benzyl.

25. The method of claim 2, wherein R is a (C_1-C_6) alkyl, aryl, or (C_2-C_9) heteroaryl.

26. The method of claim 4, wherein R is a (C_1-C_6) alkyl, aryl, or (C_2-C_9) heteroaryl.

27. A compound of the formula (VIh-1)



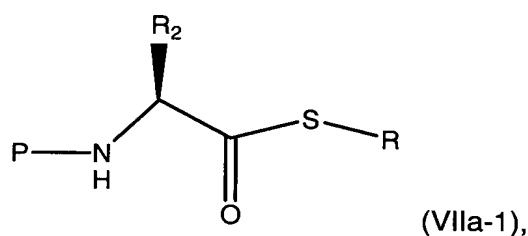
(VIh-1),

wherein:

30 P is a protecting group;

- R_2 is phenyl-(CH₂)_m-, naphthyl-(CH₂)_m-, (C₃-C₁₀)cycloalkyl-(CH₂)_m-, (C₁-C₆)alkyl or (C₂-C₉)heteroaryl-(CH₂)_m-, wherein each of said phenyl, naphthyl, (C₃-C₁₀)cycloalkyl or (C₂-C₉)heteroaryl moieties of said phenyl-(CH₂)_m-, naphthyl-(CH₂)_m-, (C₃-C₁₀)cycloalkyl-(CH₂)_m- or (C₂-C₉)heteroaryl-(CH₂)_m- groups may be optionally substituted with one, two, or three substituents independently selected from the group consisting of hydrogen, halogen, CN, (C₁-C₆)alkyl, hydroxy, hydroxy-(C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, HO-(C=O)-, (C₁-C₆)alkyl-O-(C=O)-, HO-(C=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-O-(C=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-(C=O)-O-, (C₁-C₆)alkyl-(C=O)-O-(C₁-C₆)alkyl, H(O=C)-, H(O=C)-(C₁-C₆)alkyl, (C₁-C₆)alkyl(O=C)-, (C₁-C₆)alkyl(O=C)-(C₁-C₆)alkyl, NO₂, amino, (C₁-C₆)alkylamino, [(C₁-C₆)alkyl]₂amino, amino(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)alkyl, [(C₁-C₆)alkyl]₂amino(C₁-C₆)alkyl, H₂N-(C=O)-, (C₁-C₆)alkyl-NH-(C=O)-, [(C₁-C₆)alkyl]₂N-(C=O)-, H₂N(C=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-HN(C=O)-(C₁-C₆)alkyl, [(C₁-C₆)alkyl]₂N-(C=O)-(C₁-C₆)alkyl, H(O=C)-NH-, (C₁-C₆)alkyl(C=O)-NH-, (C₁-C₆)alkyl(C=O)-[NH](C₁-C₆)alkyl, (C₁-C₆)alkyl(C=O)-[N(C₁-C₆)alkyl](C₁-C₆)alkyl, (C₁-C₆)alkyl-S-, (C₁-C₆)alkyl-(S=O)-, (C₁-C₆)alkyl-SO₂-, (C₁-C₆)alkyl-SO₂-NH-, H₂N-SO₂-, H₂N-SO₂-(C₁-C₆)alkyl, (C₁-C₆)alkylHN-SO₂-(C₁-C₆)alkyl, [(C₁-C₆)alkyl]₂N-SO₂-(C₁-C₆)alkyl, CF₃SO₃-, (C₁-C₆)alkyl-SO₃-, phenyl, phenoxy, benzyloxy, (C₃-C₁₀)cycloalkyl, (C₂-C₉)heterocycloalkyl, and (C₂-C₉)heteroaryl; and
- m is 0, 1, 2, 3, or 4.

28. A compound of the formula (VIIa-1)



wherein:

- P is a protecting group;
- R is a (C₁-C₂₀)alkyl, (C₃-C₁₀)cycloalkyl, aryl, or (C₂-C₉)heteroaryl;
- R_2 is phenyl-(CH₂)_m-, naphthyl-(CH₂)_m-, (C₃-C₁₀)cycloalkyl-(CH₂)_m-, (C₁-C₆)alkyl or (C₂-C₉)heteroaryl-(CH₂)_m-, wherein each of said phenyl, naphthyl, (C₃-C₁₀)cycloalkyl or (C₂-C₉)heteroaryl moieties of said phenyl-(CH₂)_m-, naphthyl-(CH₂)_m-, (C₃-C₁₀)cycloalkyl-(CH₂)_m- or (C₂-C₉)heteroaryl-(CH₂)_m- groups may be

optionally substituted with one, two, or three substituents independently selected from the group consisting of hydrogen, halogen, CN, (C₁-C₆)alkyl, hydroxy, hydroxy-(C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, HO-(C=O)-, (C₁-C₆)alkyl-O-(C=O)-, HO-(C=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-O-(C=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-(C=O)-O-, (C₁-C₆)alkyl-(C=O)-O-(C₁-C₆)alkyl, H(O=C)-, H(O=C)-(C₁-C₆)alkyl, (C₁-C₆)alkyl(O=C)-, (C₁-C₆)alkyl(O=C)-(C₁-C₆)alkyl, NO₂, amino, (C₁-C₆)alkylamino, [(C₁-C₆)alkyl]₂amino, amino(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)alkyl, [(C₁-C₆)alkyl]₂amino(C₁-C₆)alkyl, H₂N-(C=O)-, (C₁-C₆)alkyl-NH-(C=O)-, [(C₁-C₆)alkyl]₂N-(C=O)-, H₂N(C=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-HN(C=O)-(C₁-C₆)alkyl, [(C₁-C₆)alkyl]₂N-(C=O)-(C₁-C₆)alkyl, H(O=C)-NH-, (C₁-C₆)alkyl(C=O)-NH-, (C₁-C₆)alkyl(C=O)-[NH](C₁-C₆)alkyl, (C₁-C₆)alkyl(C=O)-[N(C₁-C₆)alkyl](C₁-C₆)alkyl, (C₁-C₆)alkyl-S-, (C₁-C₆)alkyl-(S=O)-, (C₁-C₆)alkyl-SO₂-, (C₁-C₆)alkyl-SO₂-NH-, H₂N-SO₂-, H₂N-SO₂-(C₁-C₆)alkyl, (C₁-C₆)alkylHN-SO₂-(C₁-C₆)alkyl, [(C₁-C₆)alkyl]₂N-SO₂-(C₁-C₆)alkyl, CF₃SO₃-, (C₁-C₆)alkyl-SO₃-, phenyl, phenoxy, benzyloxy, (C₃-C₁₀)cycloalkyl, (C₂-C₉)heterocycloalkyl, and (C₂-C₉)heteroaryl; and m is 0, 1, 2, 3, or 4.

29. The compound of claim 27, wherein P is carbobenzyloxy, t-butoxy carbonyl or 9-fluorenyl-methylenoxycarbonyl.

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30. The compound of claim 28, wherein P is carbobenzyloxy, t-butoxy carbonyl or 9-fluorenyl-methylenoxycarbonyl.

31. The compound of claim 29, wherein P is t-butoxy carbonyl.

25

32. The compound of claim 30, wherein P is t-butoxy carbonyl.

33. The compound of claim 27, wherein R₂ is phenyl-(CH₂)_m- or (C₂-C₉)heteroaryl-(CH₂)_m-, wherein each of said phenyl or (C₂-C₉)heteroaryl moieties may be optionally substituted with one, two, or three substituents independently selected from the group consisting of hydrogen, halogen, CN, (C₁-C₆)alkyl, or hydroxy.

30

34. The compound of claim 28, wherein R₂ is phenyl-(CH₂)_m- or (C₂-C₉)heteroaryl-(CH₂)_m-, wherein each of said phenyl or (C₂-C₉)heteroaryl moieties may be optionally

substituted with one, two, or three substituents independently selected from the group consisting of hydrogen, halogen, CN, (C₁-C₆)alkyl, or hydroxy.

- 5
35. The compound of claim 33, wherein R₂ is 3-fluoro-benzyl.
36. The compound of claim 34, wherein R₂ is 3-fluoro-benzyl.